

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-587

MICROBIOLOGY REVIEW(S)

APR 17 1996 ✓

REVIEW FOR HFD-150
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #2 OF NDA

10 April 1996

A. 1. NDA 20-587

APPLICANT Bryan Corporation
4 Plympton Street
Woburn, MA 01801

2. PRODUCT NAMES: Talc (sterile aerosol talc)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: A single-use spray can containing 4 ounces of talc

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: A pleural sclerosing agent for the relief of symptoms associated with malignant pleural effusions.

6. DRUG PRIORITY CLASSIFICATION: 1P (orphan)

B. 1. DATE OF INITIAL SUBMISSION: 11 August 1995 (subject of Microbiologist's Review #1, 16 November 1995)

2. DATE OF AMENDMENT: 24 January 1996

3. RELATED DOCUMENTS: DMF

4. ASSIGNED FOR REVIEW: 5 April 1996

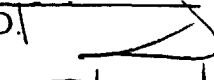
C. REMARKS: The product is for instillation into the pleural cavity. The product is to be used for pleurodesis caused by malignancies. This talc is obtained from mining operations as a mixture of ores obtained by mechanical processes. As noted in Kennedy, Vaughan and Steed (Sterilization of talc for pleurodesis; available techniques, efficacy, and cost analysis, 1995; Chest 107(4): 1032 - 1034), talc commonly is a source of *Bacillus* species, and may harbor other microorganisms including *Staphylococcus* species.

The current submission provides a proposal by to perform testing of bacteriostasis and fungistasis, microbial limits (preparatory tests), and sterility. These tests cover the bulk talc, the spray nozzle, the delivery tube and the aerosol. The current submission also addresses questions about safety of the catheter tube.

- D. CONCLUSIONS: The application is approvable pending resolution of sterility assurance issues. Questions 1 and 2 from the previous Microbiologist's Review have not been addressed and issues from question 3 remain unresolved in the current submission.

/S/

David Hussong, Ph.D.


JHC 4/17/96

cc:

HFD-150/NDA 20-587
HFD-150/CSO/D. Catterson
HFD-150/Chemist/R. Barron
HFD-805/Consult File
HFD-805/D. Hussong

Drafted by: D. Hussong, 04/10/96
R/D initialed by: P. Cooney, 04/11/96

Filename, c:\d\nda\20-587.rv2

REVIEW FOR HFD-150
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #4 OF NDA

December 22, 1997

A. 1. NDA 20-587

APPLICANT Bryan Corporation
4 Plympton Street
Woburn, MA 01801

2. PRODUCT NAMES: Sclerosol Intrapleural Aerosol (Sterile Talc Powder)
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: A single-use spray can containing 4 ounces of talc
4. METHOD(S) OF STERILIZATION:
(Isomedix)
5. PHARMACOLOGICAL CATEGORY: A pleural sclerosing agent for the relief of symptoms associated with malignant pleural effusions.
6. DRUG PRIORITY CLASSIFICATION: 1P (orphan)

- B. 1. DATE OF INITIAL SUBMISSION: 11 August 1995 (subject of Microbiologist's Review #1, 16 November 1995)
2. DATE OF AMENDMENTS: 24 January 1996 (subject of Microbiologist's Review #2); and 17 June 1997 and 6 August 1997 (subjects of Microbiologist's Review #3).
The amendment of 13 November 1997 is the subject of this review.
3. RELATED DOCUMENTS: DMF
4. ASSIGNED FOR REVIEW: 7 December 1997

- C. REMARKS: The product is instilled into the pleural cavity, for treating pleurodesis caused by malignancies. The active ingredient, talc, is obtained from mining operations and processed for cosmetics. The submission covers many changes since the previous reviews. These include the source of the raw material, the facility performing microbiology tests, the supplier of propellant, the product packaging facility, and the sterilization facility. A letter of authorization to the DMF for _____ was provided on 30 September 1997.

authorization to the DMF for
provided on 30 September 1997.

was

- D. CONCLUSIONS: The submission is approvable pending resolution of technical comments.

The Microbiologist requests that the Medical Reviewer evaluate the recommended endotoxins limit which has been proposed in this review.

/S/

12-22-97

David Hussong, Ph.D.

DK
12/22/97

cc:

HFD-150/NDA 20-587
HFD-150/CSO/D. Catterson
HFD-810/Chemist/R. Barron
HFD-805/D. Hussong

Drafted by: D. Hussong, 12/22/97
R/D initialed by: P. Cooney

Filename, c:\d\nda\20-587r4.wpd

De letter 1005

REVIEW FOR HFD-150
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW No. 1 OF NDA

16 November 1995

A. 1. NDA 20-587

APPLICANT Bryan Corporation
4 Plympton Street
Woburn, MA 01801

2. PRODUCT NAMES: Talc (sterile aerosol talc)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: A single-use spray can containing 4 ounces of talc for inhalation.

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: A pleural sclerosing agent for the relief of symptoms associated with malignant pleural effusions.

6. DRUG PRIORITY CLASSIFICATION: 1P (orphan)

B. 1. DATE OF INITIAL SUBMISSION: 11 August 1995

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: DMF

4. ASSIGNED FOR REVIEW: 25 September 1995

C. REMARKS: The product is for inhalation. The product is to be used by individuals with malignancies. Talc is obtained from mining operations as a mixture of ores obtained by mechanical processes. As noted in Kennedy, Vaughan and Steed (Sterilization of talc for pleurodesis; available techniques, efficacy, and cost analysis, 1995; Chest 107(4): 1032 - 1034), talc commonly is a source of *Bacillus* species, and may harbor other microorganisms including *Staphylococcus* species.

D. CONCLUSIONS: The application is approvable pending resolution of sterility assurance issues.

/S/

11-16-95

David Hussong, Ph.D.

[Signature] 11/17/95

cc:

HFD-150/NDA 20-587
HFD-150/CSO/D. Catterson
HFD-150/Chemist/R. Barron
HFD-805/Consult File
HFD-805/D. Hussong

Drafted by: D. Hussong, 11/14/95
R/D initialed by: P. Cooney, 11/16/95

Filename, c:\d\nda\20-587.rv1